CASE REPORT

Primary Ovarian Pregnancy After Donor Embryo Transfer: Early Diagnosis and Laparoscopic Treatment

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ABSTRACT

Primary ovarian pregnancy is a rare type of ectopic pregnancy, particularly following in vitro fertilization. Although there have been a few reported cases of primary ovarian pregnancy following in vitro fertilization embryo transfer, we believe this is the first report involving donor embryo transfer. A high index of clinical suspicion, abnormal human chorionic gonadotropin levels, and early ultrasound evaluation may aid timely diagnosis and appropriate management. This report provides a reminder to practitioners to advise patients undergoing embryo transfer of the primary ovarian pregnancy risk. Information is provided herein regarding the diagnosis and management of primary ovarian pregnancy in women treated with in vitro fertilization. We review the criteria for early diagnosis and treatment options.

Key Words: Ectopic pregnancy, Embryo donor, In vitro fertilization, Laparoscopy

INTRODUCTION

Primary ovarian pregnancy (POP) is a rare form of ectopic implantation. The incidence of natural POP ranges from 1:60 000 to 1:1 500 deliveries, accounting for 3.3% of all ectopic pregnancies.[1] Since the report of the first successful human in vitro fertilization embryo transfer (IVF-ET) cycle resulting in ectopic pregnancy, the association of ectopic pregnancy and IVF cycles has been well established. Despite the increased incidence of ectopic pregnancy associated with assisted reproductive technologies, POP is still a rare phenomenon. Following IVF-ET cycles, the overall prevalence of ovarian pregnancy has been estimated at 0.3%, representing 6% of all ectopic pregnancies.[2] With new technologies being introduced for IVF-ET in recent years, POP has been reported after some of these procedures. Thus, 3 reports highlight POP occurrence after intracytoplasmic sperm injection (ICSI) and blastocyst transfer.[3,4] Donor embryo transfer is a relatively new procedure and, to our knowledge, has not been reported in association with ovarian pregnancy.

We report a case of POP that occurred after early donor embryo transfer in a woman with no predisposing factors for ectopic implantation. This case is unique because the ovarian implantation occurred after ovarian suppression rather than with hyperstimulation, retrieval, and formation of corpora lutea cysts as reported in prior published case reports.

CASE REPORT

A 39-year-old nulligravid woman presented to our fertility center for evaluation of primary infertility. On initial examination, a transverse vaginal septum obscuring the cervix and a 1.5-cm subserosal fibroid were identified. The vaginal septum was resected. Further assessment with hysteroscopy and hysterosalpingography revealed a normal uterine cavity and tubal anatomy.

The husband was diagnosed with azoospermia and had twice undergone testicular biopsy with insufficient spermatogenesis, preventing sperm retrieval. The couple was offered intrauterine insemination or IVF-ET with donor sperm. However, these options were declined because of religious beliefs. They elected and arranged for a donor

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embryo transfer at a fertility center in their home country. The patient then had an ovarian suppression with a long protocol using Buserelin acetate and estradiol valerate. Five donor embryos were transferred with one embryo at 2-cell stage. Micronized progesterone and estradiol were initiated following the transfer.

The patient returned to our fertility center for further care. Human chorionic gonadotropin (HCG) levels were followed. The initial value was only 5 IU/L on posttransfer day 14 with an increase to 11, 27, 47 and 653 IU/L on days 16, 18, 20 and 27, respectively **(Figure 1)**. Ultrasound evaluation on day 27 showed no intrauterine gestation and normal adnexae. A repeat ultrasound was performed 8 days later after the patient experienced vaginal spotting with rising HCG. Normal adnexa and a clot in the uterus were found. On day 40, the HCG level reached 4811 IU/L. At that time, an ultrasonogram was significant for a 1.5 cm x 1.5 cm x 1.4 cm solid echogenic structure with reinforced vascular marking within to the left ovary suggesting primary ovarian pregnancy **(Figure 2)**. Our patient elected surgical management. An operative laparoscopy was performed on day 41 after transfer. Intraoperatively, the uterus and both fallopian tubes appeared normal. The left ovary was enlarged by a 3.0 cm x 2.0 cm heterogeneous mass consisting of several hemorrhagic bluish cysts, with a smooth external surface **(Figure 3)**. This mass was carefully dissected using bipolar cautery and scissors. The intact ovarian pregnancy was removed through the umbilical incision by using an endobag. Intraoperative frozen section and final histology confirmed the presence of the conception products associated with ovarian tissue. The right ovary was of normal size and color. A small amount of serous fluid was in the posterior cul-de-sac. Uterine curettage showed proliferative endometrium free of chorionic villi. Intraoperative blood loss was minimal. The patient had an uneventful postoperative recovery and was discharged the same day. Follow-up quantitative HCG levels declined appropriately and reached an undetectable level (<2 IU/L) 19 days after surgery **(Figure 1)**.

DISCUSSION

Although a rare phenomenon, primary ovarian pregnancy is an important complication associated with IVF-ET treatment. Little is known about its true incidence or risk factors. Theoretical risk factors for ovarian implantation

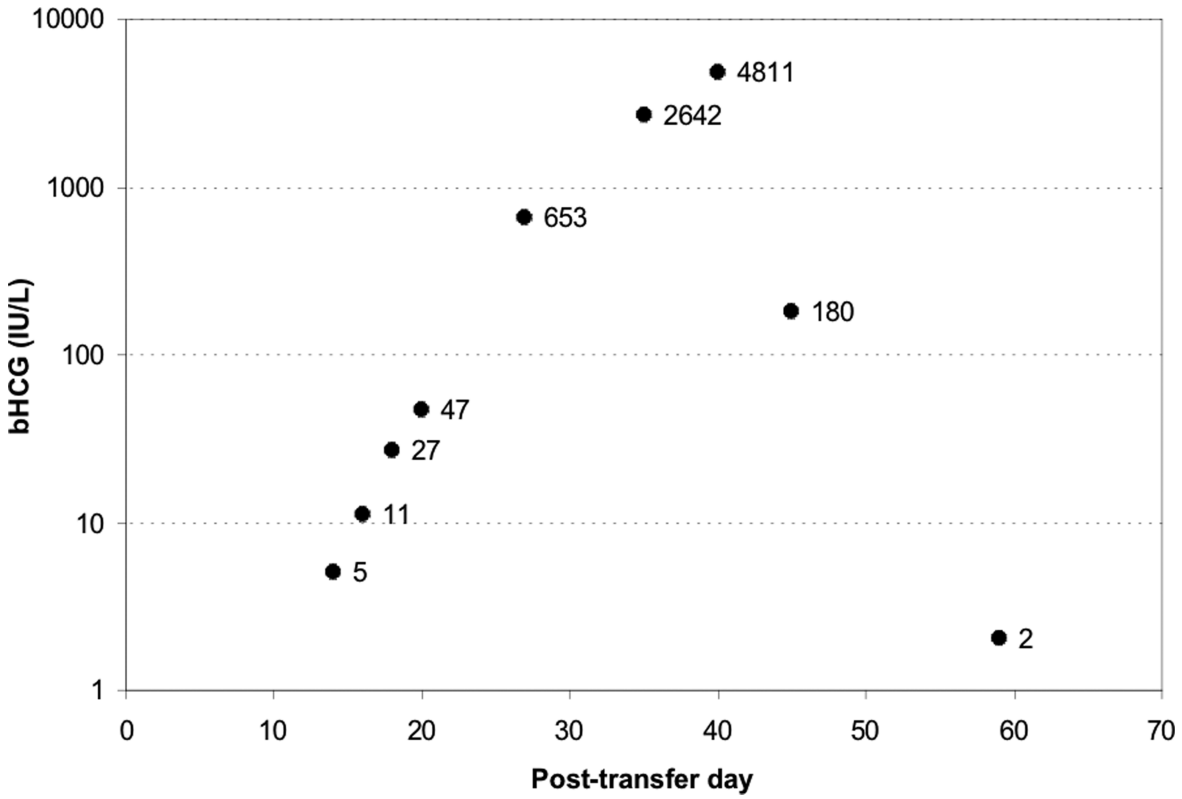

Figure 1. Course of βHCG level plotted against the number of days after embryo transfer.

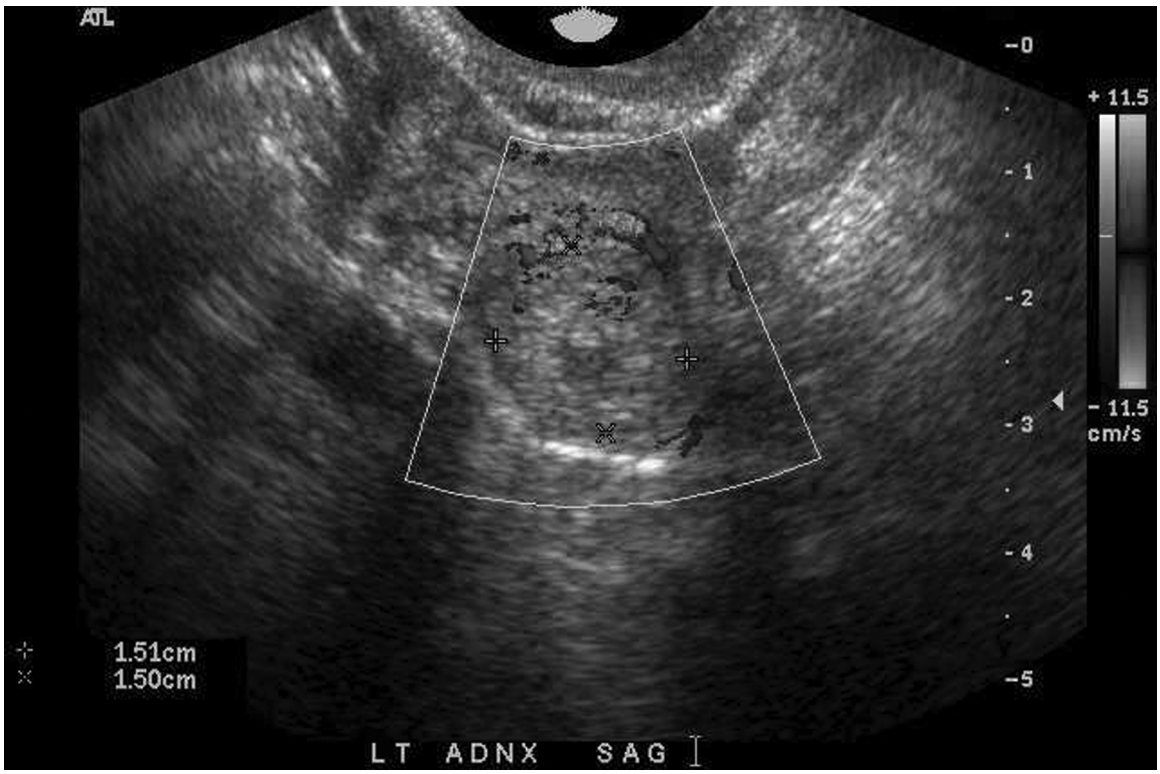

Figure 2. Transvaginal ultrasound on day 40 post embryo transfer: echogenic structure with reinforced vascular marking within the left ovary.

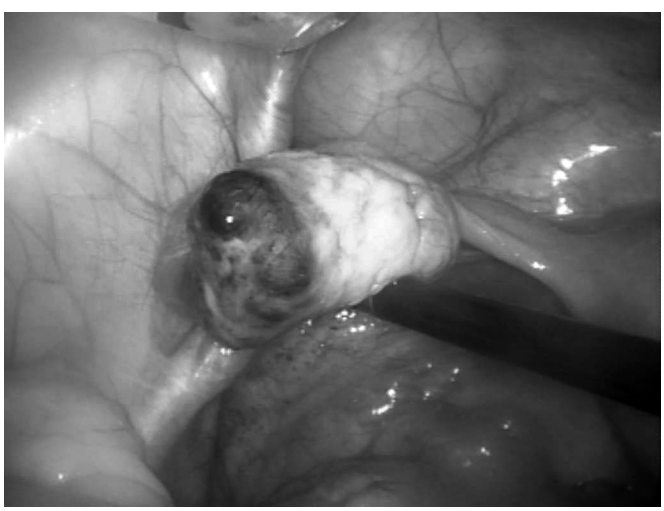

Figure 3. Photograph of the left ovary with the ovarian pregnancy (OP) at laparoscopy.

include reduction in tubal contractility as a result of high progesterone levels from multiple corpus lutea, ovarian hypervascularity after hyperstimulation and egg retrieval, excessive endometrial cavity distension with media during embryo transfer, a high number of the transferred embryos, and transfer of blastocyst.[2–6] In contrast, the donor embryo IVF cycle requires ovarian suppression, eliminating most hypothesized risk factors. However, in our case, a high number of transferred embryos is a possible explanation of ovarian implantation. Interestingly, the most frequently reported site of ovarian pregnancy is the left ovary, leaving the question of exact mechanism of retrograde embryo migration open.[1,3–4,7]

Because the occurrence of ovarian pregnancy is difficult to predict, its early recognition is imperative in patients undergoing IVF treatment. In fact, up to 50% of primary ovarian pregnancies might be diagnosed at an asymptomatic state mainly based on a physician's suspicion and experience,[2] preventing serious complications such as massive hemoperitoneum.[3] The variability of clinical signs and symptoms might be initially misleading.[3,8,9] Although not specific for ovarian pregnancy, abnormally low- and slow-rising HCG levels aid in early recognition of abnormal implantation.[2] Early use of ultrasonography in IVF programs has improved diagnosis of ovarian pregnancy.[6] The initial sonographic picture of ovarian pregnancy might be obscured by multiple corpora lutea cysts after

hyperstimulation and egg retrieval in a standard IVF-ET cycle.[7] The decisive ultrasonographic characteristics are the visualization of gestational sac structures and the presence of fetal heart beat within the ovary.[1] However, even the subtle sonographic findings, such as a round echogenic mass with reinforced vascular marking within the ovary and free peritoneal fluid, are consistent with ovarian pregnancy in case of ovarian suppression for donor embryo transfer **(Figure 2)**.

Laparoscopic management with resection of ovarian gestation and preservation of remaining ovarian tissue is the preferred treatment for ovarian pregnancy.[1–2,4,9] To avoid misdiagnosis, surgical frozen section at the time of surgery is advisable, especially when the picture of primary ovarian pregnancy is not clear.[10] Additionally, successful medical management with methotrexate as an alternative to surgery and treatment for a persistent trophoblast after laparoscopic resection of ovarian gestation has been reported.[10] However, the absence of a histopathological diagnosis needed to meet the widely accepted Spiegelberg's criteria of primary ovarian pregnancy[11] precludes using methotrexate as the first line of treatment.

CONCLUSION

It is important for clinicians and patients to recognize the possibility of developing a primary ovarian pregnancy after ovarian suppression and donor embryo transfer in an IVF program. Our case demonstrates that close follow-up of abnormally rising HCG, clinical suspicion, and sonographic appearance of an adnexal mass can lead to the early diagnosis and successful laparoscopic ovary preserving treatment.

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